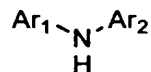


CLAIMS

What is claimed is:

1. A process for producing a diaryl amine compound of the formula (I):



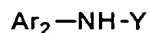
(I)

or a salt thereof,

said process comprising the step of coupling a compound of formula (II) with an amine of formula (III) in the presence of an alkali metal salt or a transition metal catalyst:



(II)



(III)

wherein:

Ar<sub>1</sub> and Ar<sub>2</sub> are independently Q;

wherein each Q is an aryl or heteroaryl ring system optionally fused to a saturated or unsaturated 5-8 membered ring having 0-4 heteroatoms;

wherein Q is optionally substituted at one or more ring atoms with one or more substituents independently selected from halo; C<sub>1</sub>-C<sub>6</sub> aliphatic optionally substituted with N(R')<sub>2</sub>, OR', CO<sub>2</sub>R', C(O)N(R')<sub>2</sub>, OC(O)N(R')<sub>2</sub>, NR'CO<sub>2</sub>R', NR'C(O)R', SO<sub>2</sub>N(R')<sub>2</sub>, N=CH-N(R')<sub>2</sub>, or OPO<sub>3</sub>H<sub>2</sub>; C<sub>1</sub>-C<sub>6</sub> alkoxy optionally substituted with N(R')<sub>2</sub>, OR', CO<sub>2</sub>R', C(O)N(R')<sub>2</sub>, OC(O)N(R')<sub>2</sub>, NR'CO<sub>2</sub>R', NR'C(O)R', SO<sub>2</sub>N(R')<sub>2</sub>, N=CH-N(R')<sub>2</sub>, or OPO<sub>3</sub>H<sub>2</sub>; Ar<sub>3</sub>; CF<sub>3</sub>; OCF<sub>3</sub>; OR'; SR'; SO<sub>2</sub>N(R')<sub>2</sub>; OSO<sub>2</sub>R'; SCF<sub>3</sub>; NO<sub>2</sub>; CN; N(R')<sub>2</sub>; CO<sub>2</sub>R'; CO<sub>2</sub>N(R')<sub>2</sub>; C(O)N(R')<sub>2</sub>; NR'C(O)R'; NR'CO<sub>2</sub>R'; NR'C(O)C(O)R'; NR'SO<sub>2</sub>R'; OC(O)R'; NR'C(O)R<sup>2</sup>; NR'CO<sub>2</sub>R<sup>2</sup>; NR'C(O)C(O)R<sup>2</sup>; NR'C(O)N(R')<sub>2</sub>;

$\text{OC(O)N(R')}_2$ ;  $\text{NR'SO}_2\text{R}^2$ ;  $\text{NR'R}^2$ ;  $\text{N(R}^2)_2$ ;  $\text{OC(O)R}^2$ ;  $\text{OPO}_3\text{H}_2$ ; and  $\text{N=CH-N(R')}_2$ ;

R' is selected from hydrogen; C<sub>1</sub>-C<sub>6</sub> aliphatic; or a 5-6 membered carbocyclic or heterocyclic ring system optionally substituted with 1 to 3 substituents independently selected from halo, C<sub>1</sub>-C<sub>6</sub> alkoxy, cyano, nitro, amino, hydroxy, and C<sub>1</sub>-C<sub>6</sub> aliphatic;

R<sup>2</sup> is a C<sub>1</sub>-C<sub>6</sub> aliphatic optionally substituted with  $\text{N(R')}_2$ , OR', CO<sub>2</sub>R', C(O)N(R')<sub>2</sub> or SO<sub>2</sub>N(R')<sub>2</sub>; or a carbocyclic or heterocyclic ring system optionally substituted with  $\text{N(R')}_2$ , OR', CO<sub>2</sub>R', C(O)N(R')<sub>2</sub> or SO<sub>2</sub>N(R')<sub>2</sub>;

wherein Ar<sub>3</sub> is an aryl or heteroaryl ring system optionally fused to a saturated or unsaturated 5-8 membered ring having 0-4 heteroatoms;

wherein Ar<sub>3</sub> is optionally substituted at one or more ring atoms with one or more substituents independently selected from halo; C<sub>1</sub>-C<sub>6</sub> aliphatic optionally substituted with  $\text{N(R')}_2$ , OR', CO<sub>2</sub>R', C(O)N(R')<sub>2</sub>, OC(O)N(R')<sub>2</sub>, NR'CO<sub>2</sub>R', NR'C(O)R', SO<sub>2</sub>N(R')<sub>2</sub>, N=C-N(R')<sub>2</sub>, or OPO<sub>3</sub>H<sub>2</sub>; C<sub>1</sub>-C<sub>6</sub> alkoxy optionally substituted with  $\text{N(R')}_2$ , OR', CO<sub>2</sub>R', C(O)N(R')<sub>2</sub>, OC(O)N(R')<sub>2</sub>, SO<sub>2</sub>N(R')<sub>2</sub>, NR'CO<sub>2</sub>R', NR'C(O)R', N=C-N(R')<sub>2</sub>, or OPO<sub>3</sub>H<sub>2</sub>; CF<sub>3</sub>; OCF<sub>3</sub>; OR'; SR'; SO<sub>2</sub>N(R')<sub>2</sub>; OSO<sub>2</sub>R'; SCF<sub>3</sub>; NO<sub>2</sub>; CN;  $\text{N(R')}_2$ ; CO<sub>2</sub>R'; CO<sub>2</sub>N(R')<sub>2</sub>; C(O)N(R')<sub>2</sub>; NR'C(O)R'; NR'CO<sub>2</sub>R'; NR'C(O)C(O)R'; NR'SO<sub>2</sub>R'; OC(O)R'; NR'C(O)R<sup>2</sup>; NR'CO<sub>2</sub>R<sup>2</sup>; NR'C(O)C(O)R<sup>2</sup>; NR'C(O)N(R')<sub>2</sub>; OC(O)N(R')<sub>2</sub>; NR'SO<sub>2</sub>R<sup>2</sup>; NR'R<sup>2</sup>;  $\text{N(R}^2)_2$ ; OC(O)R<sup>2</sup>; OPO<sub>3</sub>H<sub>2</sub>; and -N=C-N(R')<sub>2</sub>;

X is a leaving group;

Y is -C(O)-O-Z; and

Z is C<sub>1</sub>-C<sub>6</sub> aliphatic, benzyl, Fmoc, -SO<sub>2</sub>R' or Q, provided that Q is not substituted with X or alkyne.

2. The process according to claim 1, further comprising the step of removing group Y from the coupled amine to produce the compound of formula (I).

3. The process according to claim 1, wherein the process is performed using a transition metal catalyst.

4. The process according to claim 3, wherein the transition metal catalyst comprises palladium.

5. The process according to claim 4 wherein the catalyst is PdL<sub>n</sub>, wherein

each L is independently selected from -OAc, -O-tolyl, halogen, PPh<sub>3</sub>, dppe, dppf, dba, and BINAP; and n is an integer from 0-4.

6. The process according to claim 3, wherein the step of coupling a compound of formula (II) with an amine of formula (III) is performed in the presence of a base.

7. The process according to claim 6, wherein the base is selected from KOtBu, NaOtBu, K<sub>3</sub>PO<sub>4</sub>, Na<sub>2</sub>CO<sub>3</sub>, and Cs<sub>2</sub>CO<sub>3</sub>.

8. The process according to claim 1, wherein the process is performed using an alkali metal salt.

9. The process according to claim 8, wherein the alkali metal salt is selected from salts of potassium, rubidium, or cesium ions.

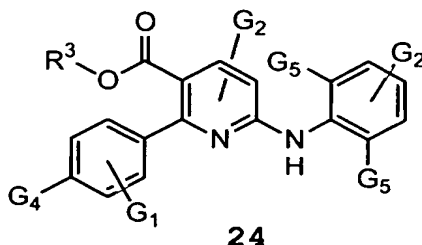
10. The process according to claim 9, wherein the alkali metal salt is selected from potassium carbonate or cesium carbonate.

11. The process according to claim 10, wherein the alkali metal salt is cesium carbonate.

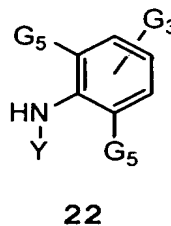
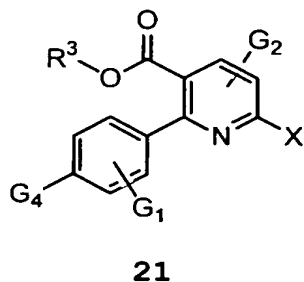
12. The process according to claim 1, wherein X is selected from the group consisting of -Cl, -Br, -I, -F, -OTf, -OTs, iodonium, and diazo.

13. The process according to claim 1, wherein Y is Boc.

14. The process according to claim 1 for producing a diaryl amine compound of the formula:



comprising the step of coupling a compound of formula **21** with an amine of formula **22** in the presence of an alkali metal salt or a transition metal catalyst:



wherein:

$R^3$  is selected from aliphatic, aryl, or aryl substituted with aliphatic, aryl, nitro, CN,  $CO_2R'$ ,  $CO_2N(R')_2$ ,  $OR'$ ,  $NCO_2R'$ ,  $NR'C(O)N(R')_2$ , and  $OC(O)N(R')_2$ ;

provided that  $R^3$  is not t-butyl; and

$G_1$ ,  $G_2$ ,  $G_3$ ,  $G_4$ , and  $G_5$  are independently selected from hydrogen, aliphatic, aryl, substituted aryl, nitro, CN, OR',  $CO_2R'$ ,  $CO_2N(R')_2$ ,  $NR'CO_2R'$ ,  $NR'C(O)N(R')_2$ ,  $OC(O)N(R')_2$ , F, Cl, Br, I, O-Tos, O-Ms,  $OSO_2R'$ , and  $OC(O)R'$ ; and

X and Y are as defined in claim 1.

15. The process according to claim 14 further comprising the step of removing group Y from the coupled amine to produce the compound of formula **24**.

16. The process according to claim 14, wherein the process is performed using a transition metal catalyst.

17. The process according to claim 16, wherein the transition metal catalyst comprises palladium.

18. The process according to claim 17 wherein the catalyst is  $PdL_n$ , wherein

each L independently is selected from -OAc, -O-tolyl, halogen,  $PPh_3$ , dppe, dppf, dba, and BINAP; and n is an integer from 0-4.

19. The process according to claim 16, wherein the step of coupling a compound of formula **21** with an amine of formula **22** is performed in the presence of a base.

20. The process according to claim 19, wherein the base is selected from KOtBu, NaOtBu,  $K_3PO_4$ ,  $Na_2CO_3$ , and  $Cs_2CO_3$ .

21. The process according to claim 14, wherein the process is performed using an alkali metal salt.

22. The process according to claim 21, wherein the alkali metal salt is selected from salts of potassium, rubidium, or cesium ions.

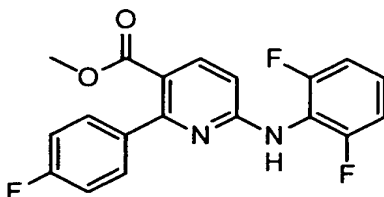
23. The process according to claim 22, wherein the alkali metal salt is selected from potassium carbonate or cesium carbonate.

24. The process according to claim 23, wherein the alkali metal salt is cesium carbonate.

25. The process according to claim 14, wherein X is selected from the group consisting of -Cl, -Br, -I, -F, -OTf, -OTs, iodonium, and diazo.

26. The process according to claim 14, wherein Y is Boc.

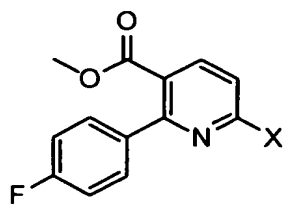
27. The process according to claim 1 for producing a diaryl amine compound of the formula:



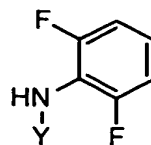
**44**

or a salt thereof,

5 said process comprising the step of coupling a compound of formula **41a** with an amine of formula **42a** in the presence of an alkali metal salt or a transition metal catalyst:



**41a**



**42a**

wherein X and Y are as defined in claim 1 above.

28. The process according to claim 27, further comprising the step of removing group Y from the coupled amine to produce the compound of formula **44**.

29. The process according to claim 27, wherein the process is performed using a transition metal catalyst.

30. The process according to claim 29, wherein the transition metal catalyst comprises palladium.

31. The process according to claim 30 wherein the catalyst is PdL<sub>n</sub>, wherein

each L is independently selected from -OAc, -O-tolyl, halogen, PPh<sub>3</sub>, dppe, dppf, dba, and BINAP; and n is an integer from 0-4.

32. The process according to claim 29, wherein the step of coupling a compound of formula **41a** with an amine of formula **42a** is performed in the presence of a base.

33. The process according to claim 32, wherein the base is selected from KOtBu, NaOtBu, K<sub>3</sub>PO<sub>4</sub>, Na<sub>2</sub>CO<sub>3</sub>, and Cs<sub>2</sub>CO<sub>3</sub>.

34. The process according to claim 27, wherein the process is performed using an alkali metal salt.

35. The process according to claim 34, wherein the alkali metal salt is selected from salts of potassium, rubidium, or cesium ions.

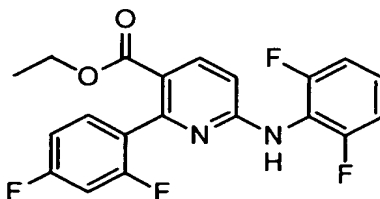
36. The process according to claim 35, wherein the alkali metal salt is selected from potassium carbonate or cesium carbonate.

37. The process according to claim 36, wherein the alkali metal salt is cesium carbonate.

38. The process according to claim 27, wherein X is selected from the group consisting of -Cl, -Br, -I, -F, -OTf, -OTs, iodonium, and diazo.

39. The process according to claim 27, wherein Y is Boc.

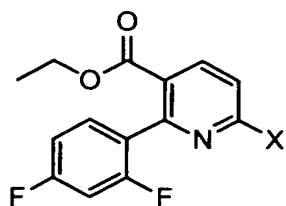
40. The process according to claim 1 for producing a diaryl amine compound of the formula:



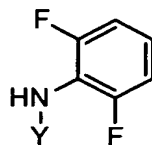
63

or a salt thereof,  
said process comprising the step of coupling a compound of formula **61a** with an amine of formula **42a** in the presence of an alkali metal salt or a transition metal catalyst:





**61a**



**42a**

wherein X and Y are as defined in claim 1 above.

41. The process according to claim 40, further comprising the step of removing group Y from the coupled amine to produce the compound of formula **63**.

42. The process according to claim 40, wherein the process is performed using a transition metal catalyst.

43. The process according to claim 42, wherein the transition metal catalyst comprises palladium.

44. The process according to claim 43, wherein the catalyst is  $\text{PdL}_n$ , wherein

each L is independently selected from -OAc, -O-tolyl, halogen,  $\text{PPh}_3$ , dppe, dppf, dba, and BINAP; and n is an integer from 0-4.

45. The process according to claim 42, wherein the step of coupling a compound of formula **61a** with an amine of formula **42a** is performed in the presence of a base.

46. The process according to claim 45, wherein the base is selected from KOtBu, NaOtBu,  $\text{K}_3\text{PO}_4$ ,  $\text{Na}_2\text{CO}_3$ , and  $\text{Cs}_2\text{CO}_3$ .

47. The process according to claim 40, wherein the process is performed using an alkali metal salt.

48. The process according to claim 47, wherein the alkali metal salt is selected from salts of potassium, rubidium, or cesium ions.

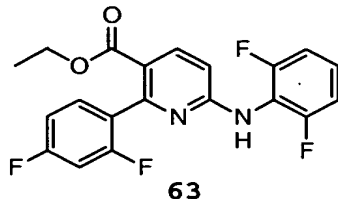
49. The process according to claim 48, wherein the alkali metal salt is selected from potassium carbonate or cesium carbonate.

50. The process according to claim 49, wherein the alkali metal salt is cesium carbonate.

51. The process according to claim 40, wherein X is selected from the group consisting of -Cl, -Br, -I, -F, -OTf, -OTs, iodonium, and diazo.

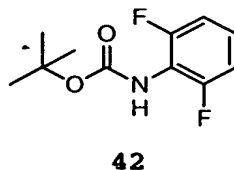
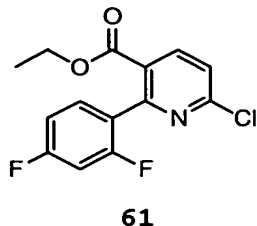
52. The process according to claim 40, wherein Y is Boc.

53. The process according to claim 40 for producing a diaryl amine compound of the formula:



or a salt thereof,

said process comprising the step of coupling a compound of formula **61** with an amine of formula **42** in the presence of a suitable alkali metal salt or transition metal catalyst:



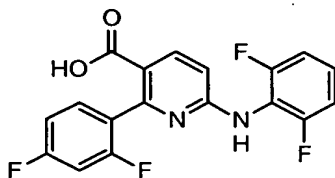
54. The process according to claim 53 further comprising the step of removing the Boc group from the coupled amine to produce the compound of formula **63**.

55. The process according to any of claims 53 or 54 wherein the process is performed using cesium carbonate.

56. The process according to claim 54 further comprising the steps of:

(a) reacting the compound of formula **63** with a base; and

5 (b) acidifying the reaction mixture formed in step (a) to produce a compound of the formula **75**:



**75**

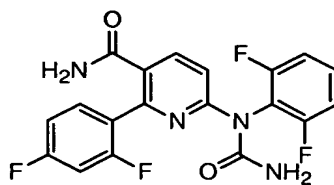
57. The process according to claim 56 wherein the base in step (a) is NaOH.

58. The process according to claim 56 wherein the acid in step (b) is HCl.

59. The process according to claim 56 further comprising the steps of:

(c) reacting the compound of formula **75** with diphosgene; and

5 (d) treating the reaction mixture formed in step (c) with  $\text{NH}_4\text{OH}$  to produce a compound of the formula **76**:



**76**